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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
07/488,307	03/05/90	GREGORY R	IG490

EXAMINER
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ART UNIT	PAPER NUMBER
1806	8

DATE MAILED: 01/21/93

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

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Response Due 4/21/93

☒ This application has been examined ☒ Responsive to communication filed on 9/23/92 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire three month(s), ____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims ~~1-98~~ 1-45, 64-82, 85, 87, 89-98 are pending in the application.
   Of the above, claims 1-45, 64-82, 85, & 87 are withdrawn from consideration.
2. ☒ Claims 46-63, 83-84, 86, & 88 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 89-98 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

Part III DETAILED ACTION

15. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

16. Applicant's election without traverse of Group I in Paper No. 7, filed September 23, 1992, is acknowledged.

17. Claims 89-98 are rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Wilson.

The claims recite generically a variety of cystic fibrosis membrane conductance regulators which are essentially claimed in product by process form. As it is a well established principle that the process by which a product is made does not alter the product per se.

The Wilson reference provides a methods for the purification and isolation of the Cystic Fibrosis Protein (CFP) are also disclosed, see for example the last sentence of the abstract. See also the bottom of column 4 bridging to column 5 where specific protocols for the isolation and purification of CFP are disclosed. In so far as the claims are not limited in any way to the type of transmembrane regulator, the reference anticipates the claims as filed. Applicants are invited to provide a showing that the instant protein of Wilson is not the same as that of applicants invention.

In the alternative that applicants should show that the instant protein of the Wilson application is not the same as applicants, the production of such broad claims as that of the instant invention would be rendered obvious given the explicit teaching of Wilson for the production of monoclonal antibodies for the isolation of any cystic fibrosis proteins. See for example lines 25-46 of column 6.

In response, applicants have argued that the rejection cannot be maintained under §102 because the Wilson patent states that the antibodies do not bind to normal serum. Because applicant's CFTR is found in normal serum and cystic fibrosis serum, applicants reason that the CFP taught by Wilson cannot be the CFTR of the instant claims. Such logic has been considered but is unpersuasive because the Wilson patent teaches a method of discriminating between the normal cystic fibrosis gene and the mutant version, which causes cystic fibrosis. Therefore, the antibodies of Wilson will be expected to bind to the epitope formed by the mutation to the gene. Because the mutated gene and hence the protein which results from the gene will have unique epitopes to which antibodies can bind, the Wilson antibodies could very well bind to diseased or mutated individuals only.

Moreover, Wilson was trying to find antibodies which would discriminate between the mutant protein and the native protein. Therefore, the fact that the antibodies bind to only the diseased serum was in keeping with the Wilson's intent, which was a method of diagnosis. Therefore, the fact that the antibodies of Wilson only bound to diseased serum is not conclusive evidence that the CFP taught by the prior art is not the CFTR of the instant claims. Arguments concerning the recombinant nature of the expression product amount to product by process arguments which do not materially alter the identity of the product which applicants have broadly claimed. Burden is placed on applicants to show that the CFP of Wilson is not the CFTR of the instant invention.

18. Claims 89-98 are rejected under 35 U.S.C. § 103 as being unpatentable over Riordan et al in view of Harris and Carrier.

The scope of the instant claims has been discussed supra.

The Riordan reference teaches the consensus cDNA sequence for the CFTR protein of the instant invention. The predicted amino acid sequence and the secondary structure of the expression product are also predicted in the Riordan disclosure giving one of ordinary skill in the art sufficient knowledge for the synthesis of the full length cDNA. Riordan lacks the actual expression of the cDNA, nor has the cDNA actually been isolated. However, these distinctions are not considered patentable because the once the DNA sequence of the gene is known DNA synthesizers exist within ordinary skill in the art for the synthesis of a gene, given the sequence. Also, primers might be synthesized which would be useful for the screening of cDNA libraries for the isolation of either the genomic or cDNA sequence. Such techniques are within the purview of the skilled artisan. Should applicant question the capability of such techniques, references will be supplied to support the assertion. The lack of expression of the cDNA of Riordan is not considered of patentable import because applicants constructs have not been expressed either. Since the instant specification fails to provide examples showing expression of the cDNA of Riordan, the expression of the known and disclosed cDNA sequence of Riordan for the production of a functional protein is considered within the ordinary skill of the art.

In response, applicants argue that the even though a single cDNA sequence might have been constructed from overlapping plasmid, such an approach did not work as evidenced by applicant's own specification as well as the citation of Tsui et al which states that the instability of the DNA sequence. Such instability is considered to be a limiting factor in the ability of applicants to express the cDNA to obtain the claimed CFTR protein. The solution to such instability, applicants assert, is the invention

and so results in the patentability of the instant invention. Final arguments conclude a single DNA sequence would not be synthesized because of the difficulty associated with the synthesis of such a large gene. Applicant's arguments filed 9/23/92 have been fully considered but they are not deemed to be persuasive.

The generation of the expression product as evidenced by Tsui reference is unpersuasive because the problem encountered was a relatively routine one in which the expression product (protein) was toxic to the host cell. The reason for such toxicity is generally the over-production of the protein which overwhelms the host cell an kills it. A simple strategy to resolve such a problem is the use of low copy number plasmids as stated by the Tsui reference. The use of such technology is old and well known and is evidenced by the Harris reference which is incorporated into the rejection. Note the bottom of page 102 where the reference teaches the relatively straightforward task of generating an amino acid sequence from a DNA sequence and constructing either the protein or the gene from the sequence information. Additionally, the Carrier reference teaches on page 110, first paragraph that high copy number plasmids can be dangerous to protein production through host cell toxicity. The reference suggests using temperature sensitive plasmids to control copy number, however, using simple low copy number plasmid would also suffice. In conclusion, given knowledge that plasmid instability was a problem, the use of common techniques for the resolution of such instability is not considered to be a patentable distinction.

19. Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). The practice of automatically extending the shortened statutory period an additional month upon the filing of a timely first response to a final rejection has been discontinued by the Office. See 1021 TMOG 35.

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Nisbet whose telephone number is (703) 308-4204. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

TMN
January 12, 1993

DAVID L. LACEY
SUPERVISORY PATENT EXAMINER
GROUP 180
1/13/93